SUPPLEMENTAL MATERIAL

Animal Use and Lessons Learned in the
U.S. High Production Volume Chemicals Challenge Program

Patricia L. Bishop[1], Joseph R. Manuppello[1], Catherine E. Willett[1], Jessica T. Sandler[1]

[1]People for the Ethical Treatment of Animals, Regulatory Testing Division, Norfolk, VA, 23510

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APO comments on the second and third proposed Section 4 TSCA (Toxics Substances Control Act) test rules that reduced animal testing.

Animal Protection Organizations (APOs) submitted comments to EPA regarding High Production Volume (HPV) chemicals proposed for testing under Section 4 TSCA, a number of which resulted in reduction of animal testing or elimination of the chemical entirely from the test rule. Several examples are given below.

1. In comments submitted to EPA (Manuppello et al. 2008) for the proposed TSCA Section 4 test rule on the second group of HPV chemicals (U.S. EPA 2008), APOs stated that reproductive and developmental toxicity testing was not needed for 2,4-hexadienoic acid, (E,E)- (also known as sorbic acid), as several multi-generation studies in mice and rats (e.g., Demaree et al. 1955; Gaunt et al., 1975) reported no adverse effects of sorbic acid on reproductive function or post-natal development. The APO comments additionally cited the Food and Drug Administration (FDA) as listing sorbic acid as Generally Recognized as Safe (GRAS) as a preservative for direct addition to food. In its response (U.S. EPA 2010a), EPA reviewed the cited studies and acknowledged there was no evidence suggesting the chemical was either a reproductive or developmental toxicant, but did not make reference to the GRAS classification, which, in all likelihood, should have excluded this chemical from testing altogether. The agency stated it "…is not finalizing the reproduction/developmental toxicity screening test", but maintained that data on aquatic toxicity would still have to be developed (EPA 2010a).

2. Also in comments on the second proposed test rule (Manuppello et al. 2008), APOs noted that information existed (e.g., Goldman et al. 1977; Sheik-Omar and Scheifer 1980; Lamb et al. 1997) on the reproductive and developmental effects of ethanedioic acid (also known as oxalic acid) from several studies, including data from the National Toxicology Program (NTP 1985), thus obviating the need for reproductive/developmental toxicity testing. EPA reviewed the NTP study and noted in its response that while it did "…not conform entirely to current OECD reproductive and developmental testing guidelines, upon further consideration, it is considered adequate to eliminate the need for further reproductive and developmental testing under a test rule" (U.S. EPA 2010a).

3. The third proposed test rule (U.S. EPA 2010b) required mammalian acute toxicity and combined repeated-dose reproduction/developmental toxicity screening tests for Benzene, 1,2-dimethyl-3-nitro- (3-NOX). In comments (Manuppello 2010), APOs referenced an abstract (Anonymous 1994) from a 1994 German toxicology assessment in the TOXLINE database (U.S. NLM 2011) that summarized results of oral acute and repeated dose toxicity studies of 3-NOX in rats. Upon examination of the studies, EPA determined that they provided sufficient information to adequately characterize the acute and repeated dose hazards of oral exposure to 3-NOX (U.S. EPA 2011).

4. EPA called for reproductive/developmental toxicity testing of 3-pentanone in its third proposed test rule (U.S. EPA 2010b). With regards to 3-pentanone, APOs urged EPA in their comments (Manuppello 2010) to consider the existing data for 2-pentanone, a structurally similar chemical that was already sponsored in the HPV Challenge program and for which all health effects endpoints were fulfilled. EPA stated in its response (U.S.

EPA 2011) that it assessed the existing data for 2-pentanone, and based on similar chemical/physical properties and comparative acute lethality data, considered a read-across approach from 2-pentanone to 3-pentanone to be appropriate. EPA further stated that toxicity data submitted for 2-pentanone were adequate to satisfy all testing requirements for 3-pentanone, and it would drop the chemical from the test rule (U.S. EPA 2011).

TSCA Updates

Bills that would significantly rewrite TSCA have been introduced three times since 2008 (Kid Safe Chemicals Act of 2008; Safe Chemicals Act of 2010; Safe Chemicals Act of 2011) and though none have received much support in Congress, each would change the legislation to look more like the European REACh (Registration, Evaluation, Authorization and Restriction of Chemical Substances) Program (European Commission 2006) by requiring information on more chemicals and toxicological endpoints. The latest versions contain language that promotes minimization of animal testing and supports development of non-animal assessment approaches, but other elements of these drafts are still contentious and subject to further discussion and amendment. By the time TSCA legislation is revised in the U.S., information for at least the first two categories of REACh likely will have been generated, as the deadline for substances produced or imported at greater than 100 tonnes per year is December 2013 (European Commission 2006). Any revision of TSCA should take this into account and allow use of this information to the greatest extent possible.

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